Preparation and Evaluation of Sustained release Curcumin Loaded Solid Lipid Nanoparticles

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- Iran is home to one of the world's oldest continuous major civilizations, with historical and urban settlements dating back to 4000 BC.
- Tehran is the capital of Iran. Tehran is the largest city and urban of Iran, the 2nd-largest city in Western Asia, and the 3rd-largest in the Middle East.
Currently, IAUPS is the only Pharmaceutical Branch in Tehran providing educational, research, and technological services and programs as a unique branch of Islamic Azad University. This university offers BS, MSc, Pharm D and PhD programs for students to serve the very goal of education and research and obtain the objections regarding development in different fields such as Pharmacy, Medicinal Chemistry, Biotechnology, Nanotechnology, Microbiology, Phytochemistry etc.
Introduction

• Recently phytotherapeutics were prepared in nano size to improve pharmacokinetic and pharmacodynamics characteristics.
Nanoparticles

- Nanoparticles (NPs) are colloidal particles in which the active ingredients are dissolved, entrapped in and/or is adsorbed or attached on to the particle.
Advantages of nanotechnology in phytoceuticals

- The probability of designing sustained release systems,
- Enhanced physicochemical stability,
- Enhanced permeability,
- Improves tissue distribution
- and Enhanced solubility and bioavailability
Curcumin, a phenolic compound from the plant Curcuma Longa as a traditional spice have many pharmacological activities including:

- anti-diabetic,
- anti-inflammatory,
- anti-cancer,
- anti-oxidant,
- antibacterial,
- anti-HIV
- anti-aging activity
- hepatoprotective activity
- cardiovascular benefits.
Antibacterial activities of Curcumin

The antibacterial study on aqueous extract of C. longa rhizome was carried out on:

- S. epidermis
- Staph. aureus
- Klebsiella pneumoniae
- E. coli
- methicillin-resistant Staph. aureus strains (MRSA)
- And .....
NDDS and Curcumin

• Many novel drug delivery strategies have been described to increase solubility, bioavailability and delivery of curcumin including:
  • liposomes,
  • Nano- or micro- emulsions,
  • Polymeric NPs
  • Solid Lipid NPs,
  • Polymer conjugates,
  • Polymeric micelles,
  • Nanocrystals
  • Nanogels etc.
Advantages of SLNs

- Biocompatibility,
- Good tolerability, and
- Ease of scale-up
- Possibility of loading water soluble and insoluble molecules
- Used as carrier to sustain the release of drugs
Preparation of Curcumin SLNs

- Curcumin loaded SLNs were prepared using high pressure homogenization technique as described below:
- 0.1 g tween 80 and 600 mg curcumin were added to 10 ml of purified water at room temperature,
- 600 mg of cholesterol was dissolved in mixture of ethanol and acetone on 3-1 ratio at 75-80 °C,
- then the hot oily phase was added to aqueous phase under homogenization at 11000 rpm and the mixture was homogenized for 7 minutes.
- While the mixture cooled to room temperature, SLNs formed
Particle size analysis

- The evaluation of particle size was done using Malvern zeta sizer (ZEN3600) and confirmed by scanning electron microscopy (SEM). Optimized SLNs had 112 and 163 nm particle size before and after freeze drying.
Measurement of drug loading efficiency

- For determination of drug loading efficacy (LE%) of curcumin solid lipid nanoparticles, the samples were centrifuged at 26,000 rpm for 35 minutes at -4 °C using Sigma laboratories centrifuge.
- Concentration in the supernatant was analyzed using UV spectrophotometer at 424 nm and LE% was calculated using reverse method applying following equation.
- Results show that the LE% was equal to 70.4±1.2%.

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\text{Drug Loading efficacy (LE %)} = \frac{\text{Drug}_{\text{total}} - \text{Drug}_{\text{supernatant}}}{\text{Drug}_{\text{total}}} \times 100
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Drug release study

• Release study was performed using dialysis sack method by DO405 dialysis tubing 23-15mm.
• 5 ml of each formulation was placed in dialysis membrane and immersed in 50 ml phosphate buffer pH 7.4 containing 0.1% Tween 80.
• Two ml samples were withdrawn in predetermined time intervals and drug concentration was measured at 424 nm.
• To ensure that sustained release profile is not due to membrane, curcumin dispersion in the same concentration with curcumin SLNs was studied under the same condition for release.
Freeze drying

- To increase stability and shelf life, curcumin SLNs were lyophilized successfully. Lyophilization was done by using 5 and 15% mannitol as cryoprotectant at freezing temperature equal to -20°C for 24 hours and then particles were lyophilized for 48 hours by freeze-dryer (Lyotrap/Plus, UK) at -40°C and pressure equal to 0.4 bar. After freeze drying size enlargement was not occurred.
DSC Analysis

- To ensure about sustained profile of release, DSC thermograms were obtained using (Mettler, Switzerland). Certain amount of dried nanoparticle powder was crimped in a standard aluminum pan and heated from 25 to 400 °C at a heating rate of 10 °C/min under constant heating.
DSC Analysis Result

- DSC thermograms of pure cholesterol, curcumin and curcumin-loaded SLNs show that melting point of cholesterol has shifted from 80 °C to about 170 °C in the SLNs of curcumin. The melting temperature of curcumin is also seen at 185 °C in the thermogram of pure curcumin.

- Chemical structure of curcumin and cholesterol could support probability of hydrogen band formation between these two compounds which resulted in prolonged release from nanoparticles.
To compare the antimicrobial activity of curcumin loaded nanoparticles with free curcumin, “well diffusion test” was carried out using E. coli (ATCC 25922) as the Gram-negative pathogenic strain and S. aureus (ATCC 25923) as Gram positive strain. In this study SLNs without curcumin was studied as blank.
Synergic antibacterial effect

• Now we are working on synergic antibacterial effect of desired Curcumin SLNs with SLNs of chemical antibacterial compounds to overcome antibiotic resistance species with present antibiotics and slow down the need of new antibiotic generations.
References


Thank you for your attention
Any question?